



TITLE:

Successful recovery from interstitial pneumonitis, induced by bicalutamide and leuprorelin acetate given as treatment for prostate cancer

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SUCCESSFUL RECOVERY FROM INTERSTITIAL PNEUMONITIS, INDUCED BY BICALUTAMIDE AND LEUPRORELIN ACETATE GIVEN AS TREATMENT FOR PROSTATE CANCER

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We report a case of interstitial pneumonitis induced by bicalutamide and/or leuporelin acetate given as therapy for prostate cancer, in which the pneumonitis was successfully managed by steroid treatment. Steroids were given promptly on the day following onset of pneumonitis, and the patient (72 years old) recovered almost completely within one and a half months. Interstitial pneumonitis, induced by hormone treatment given for prostate cancer, is a reversible condition and a quick diagnosis followed by prompt, proper treatment is important to ensure a successful recovery. The patient had been free of interstitial pneumonitis for 14 months, but died of pneumothorax.

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Key words : Interstitial pneumonitis, Maximal androgen blockade therapy, Prostate cancer

INTRODUCTION

Maximal androgen blockade therapy (MAB), with an antiandrogen and luteinizing hormone-releasing hormone (LH-RH) agonist, is now standard endocrine treatment for advanced prostate cancer. Interstitial pneumonitis is an extremely rare adverse reaction to this therapy, and only a few cases have been reported in the literature^{1–6)}. In this report we highlight how a quick diagnosis and a prompt treatment resulted in a complete recovery from interstitial pneumonitis.

CASE REPORT

A 72-year-old man, with a 2-month history of prostate cancer, was referred to our emergency room in February 2003 with severe dyspnea. In December 2002, at another hospital, prostate specific antigen (PSA) levels of 800 ng/ml had been detected in this patient. A prostate biopsy and bone scan performed at the time, revealed a poorly differentiated adenocarcinoma (Gleason score ; 4+5) with multiple bone metastases. The patient received hormone treatment with fosfestrol (300 mg/day), by intravenous drip infusion for 10 days. Then, in January 2003, MAB therapy, oral bicalutamide (80 mg/day) and depot leuporelin acetate (3.75 mg by subcutaneous injection once a month) treatment was started with bicalutamide 2 weeks before the first depot injection of leuporelin acetate. In the evening following his second leuporelin acetate injection, the patient presented at our hospital having suddenly developed breathing difficulties. Lung auscultation revealed bilateral fine crackles. Arterial blood gas showed an oxygen partial pressure of only 49.0 mmHg. Chest x-rays showed bilateral, diffuse

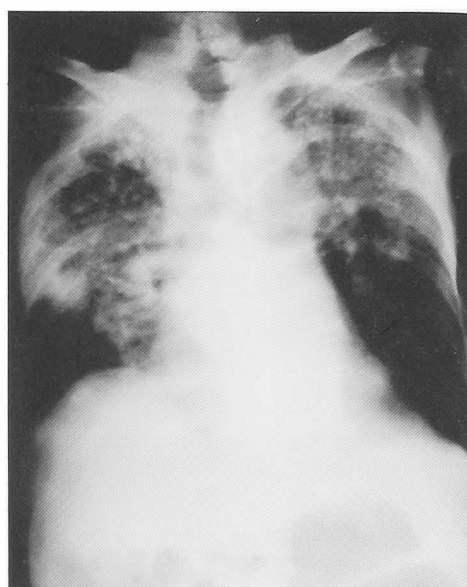


Fig. 1. Chest X-ray shows diffuse bilateral reticulonodular infiltration.

reticulonodular shadowing, especially in the upper lung fields (Fig. 1), which was confirmed by a chest computed tomography scan (Fig. 2). Because the pulmonary shadow had spread to the lower lung fields by the next day, the patient received steroid pulse therapy (methylprednisolone sodium succinate 1,000 mg for 3 days), followed by respiratory assistance via a respirator. However, as the patient's respiratory condition did not improve, he started a second steroid pulse treatment on Day 17, after which his breathing difficulties gradually resolved and he was taken off the respirator. A chest x-ray taken on Day 45, showed a marked improvement (Fig. 3). Once his interstitial pneumonitis had improved, on Day 80, the patient underwent an orchiectomy,

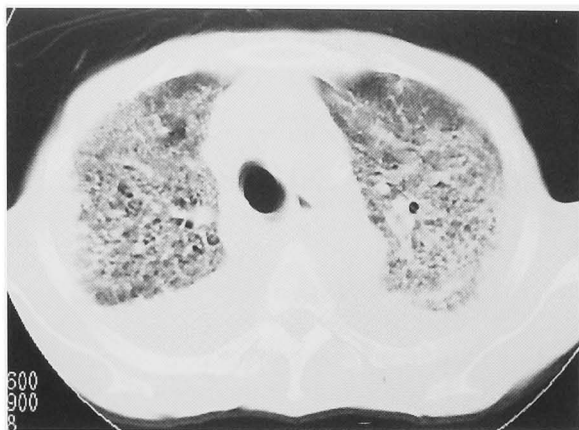


Fig. 2. Computed tomography of chest shows reticulonodular pattern.

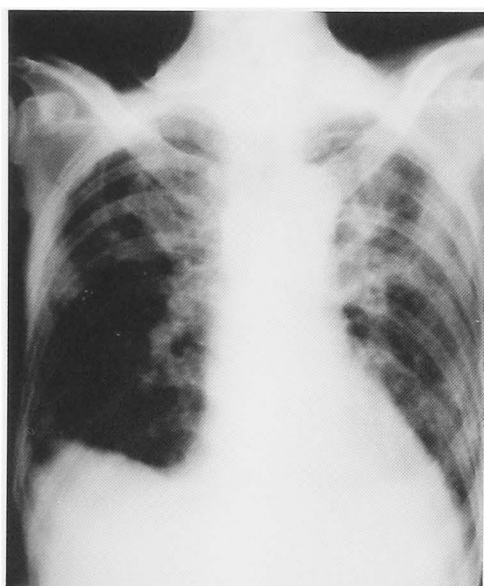


Fig. 3. Chest X-ray shows marked improvement.

however, his PSA levels have since gradually increased to over 800 ng/ml. The patient has now been completely clear of interstitial pneumonitis over 12 months (Fig. 4). However, the patient presented with suddenly developed dyspnea again in May 2004. The patient was diagnosed as having pneumothorax



Fig. 4. Computed tomography of chest shows no reticulonodular pattern.

and died of it. There was no autopsy.

DISCUSSION

Maximal androgen blockade (MAB, antiandrogen and LH-RH agonists) is now the standard endocrine treatment for advanced prostate cancer. Interstitial pneumonitis is an uncommon, but severe adverse reaction to this therapy. Both non-steroidal antiandrogens and LH-RH agonists have been reported to induce interstitial pneumonitis¹⁻⁶. In the case report discussed here, the patient developed severe dyspnea just after he received his second LH-RH injection, with leuporelin acetate, suggesting that it was the LH-RH agonist that was responsible for the interstitial pneumonitis. Generally, interstitial pneumonia is caused by some kinds of collagen diseases, radiation and many kinds of drugs. The reported incidence of drug-induced lung disease is 6-7% of all drug-induced side effects, and of this 6-7%, interstitial pneumonia accounts for about 60%. The standard treatment is steroid therapy, immune suppressive drugs and use of a respirator. There is no special feature of the drug-induced interstitial pneumonia⁷. From radiological findings, we promptly diagnosed this as a case of MAB-induced interstitial pneumonitis and started steroidal treatment on the day after onset. After two courses of steroid therapy the pneumonitis had completely resolved. Therefore, a quick diagnosis and proper treatment resulted in a successful recovery from MAB-induced interstitial pneumonitis. The patient recovered from interstitial pneumonitis, however he died of pneumothorax. It was considered that interstitial pneumonitis induced bulla, spontaneous rupture of which resulted in fatal pneumothorax. We have reported previously a similar case of MAB-related interstitial pneumonitis⁶, where fosfestrol was also administered before MAB treatment⁶. Nevertheless, although in both cases, interstitial pneumonitis developed approximately one month after MAB treatment, we cannot say with any certainty that it was the change from fosfestrol to MAB treatment that induced the onset of interstitial pneumonitis.

In conclusion, interstitial pneumonitis is an extremely rare, but reversible, adverse reaction to MAB treatment. Physicians should be aware of this type of pneumonitis in order that the correct treatment can be promptly initiated, thus maximizing the chances of full recovery.

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和文抄録

ステロイド治療により軽快した前立腺癌内分泌療法による間質性肺炎の1例

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前立腺癌の内分泌療法においては稀な副作用として間質性肺炎がある。前立腺癌によるホルモン療法による間質性肺炎と診断、ステロイド治療により軽快した間質性肺炎の1例を経験した。前立腺癌のホルモン療法による間質性肺炎の治療には、迅速な診断とステロ

イド治療の早期開始が重要と考えられる。間質性肺炎の治療経過は良好であったが、器質化した肺が気胸を起こし、死亡に至った。

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